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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/853,033	05/11/2001	Pierre Chambon	065691-0222	5081

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EXAMINER

QIAN, CELINE X

ART UNIT PAPER NUMBER

1636

DATE MAILED: 12/28/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

**Advisory Action**

Application No.

09/853,033

Applicant(s)

CHAMBON ET AL.

Examiner

Celine X Qian Ph.D.

Art Unit

1636

--The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

THE REPLY FILED 16 November 2004 FAILS TO PLACE THIS APPLICATION IN CONDITION FOR ALLOWANCE. Therefore, further action by the applicant is required to avoid abandonment of this application. A proper reply to a final rejection under 37 CFR 1.113 may only be either: (1) a timely filed amendment which places the application in condition for allowance; (2) a timely filed Notice of Appeal (with appeal fee); or (3) a timely filed Request for Continued Examination (RCE) in compliance with 37 CFR 1.114.

**PERIOD FOR REPLY** [check either a) or b)]

- a) ☒ The period for reply expires 3 months from the mailing date of the final rejection.
- b) ☐ The period for reply expires on: (1) the mailing date of this Advisory Action, or (2) the date set forth in the final rejection, whichever is later. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of the final rejection. ONLY CHECK THIS BOX WHEN THE FIRST REPLY WAS FILED WITHIN TWO MONTHS OF THE FINAL REJECTION. See MPEP 706.07(f).

Extensions of time may be obtained under 37 CFR 1.136(a). The date on which the petition under 37 CFR 1.136(a) and the appropriate extension fee have been filed is the date for purposes of determining the period of extension and the corresponding amount of the fee. The appropriate extension fee under 37 CFR 1.17(a) is calculated from: (1) the expiration date of the shortened statutory period for reply originally set in the final Office action; or (2) as set forth in (b) above, if checked. Any reply received by the Office later than three months after the mailing date of the final rejection, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

1. ☐ A Notice of Appeal was filed on \_\_\_\_\_. Appellant's Brief must be filed within the period set forth in 37 CFR 1.192(a), or any extension thereof (37 CFR 1.191(d)), to avoid dismissal of the appeal.
2. ☒ The proposed amendment(s) will not be entered because:
- (a) ☐ they raise new issues that would require further consideration and/or search (see NOTE below);
- (b) ☐ they raise the issue of new matter (see Note below);
- (c) ☒ they are not deemed to place the application in better form for appeal by materially reducing or simplifying the issues for appeal; and/or
- (d) ☒ they present additional claims without canceling a corresponding number of finally rejected claims.

NOTE: See Continuation Sheet.

3. ☐ Applicant's reply has overcome the following rejection(s): \_\_\_\_\_.
4. ☐ Newly proposed or amended claim(s) \_\_\_\_\_ would be allowable if submitted in a separate, timely filed amendment canceling the non-allowable claim(s).
5. ☒ The a) ☐ affidavit, b) ☐ exhibit, or c) ☒ request for reconsideration has been considered but does NOT place the application in condition for allowance because: See Continuation Sheet.
6. ☒ The affidavit or exhibit will NOT be considered because it is not directed SOLELY to issues which were newly raised by the Examiner in the final rejection.
7. ☒ For purposes of Appeal, the proposed amendment(s) a) ☐ will not be entered or b) ☐ will be entered and an explanation of how the new or amended claims would be rejected is provided below or appended.

The status of the claim(s) is (or will be) as follows:

Claim(s) allowed: \_\_\_\_\_.

Claim(s) objected to: \_\_\_\_\_.


Claim(s) rejected: 1, 4-8, 10-12, 14, 19, 23, 33, 50 and 52.

Claim(s) withdrawn from consideration: 9, 13, 15-18, 21, 22, 24-32, 35-49, 51 and 53-61.

8. ☐ The drawing correction filed on \_\_\_\_\_ is a) ☐ approved or b) ☐ disapproved by the Examiner.
9. ☐ Note the attached Information Disclosure Statement(s) (PTO-1449) Paper No(s). \_\_\_\_\_.
10. ☐ Other: \_\_\_\_\_

Continuation of 2. NOTE: The proposed amendment does not overcome the rejection of record. The arguments are not persuasive to overcome the 112 1st rejection and 103 rejection raised in the final office action (see reasons below). Further, the newly added claims 64 and 65 are directed to a transgenic mouse line aP2-Cre-ER T2/RXRaL2/-, which was not examined because it is not directed to elected subject matter. These claims raise new issues that would require further consideration. Therefore, the proposed amendment will not be entered.

Continuation of 5. does NOT place the application in condition for allowance because: these arguments does not overcome the rejection of the record mailed on 6/16/04. In response to the 112 1st paragraph rejection, Applicants argue that all of the mice of the present invention have a predictable primary phenotype which allows one skilled in the art to detect such mice and to distinguish them from wild type mouse. However, such phenotype is not recited in any of the rejected claims. As such, the claims does not contain essential elements that are required for the enablement of the claimed invention. Therefore, this rejection is maintained for same reasons discussed in the final office action. In response to the 103 rejection, Applicants argue that the combined teaching lack expectation of success to obtain a system that works with 100% deletion efficiency. Applicants further argue that extraordinary skill was required to obtain the present invention based on the teaching of Feil since Applicants are the first to obtain the claimed invention four years after the Feil publication. In response to these arguments, Applicants are reminded that the alleged 100% deletion efficiency or tight temporal control of the generation of cell type/tissue-specific somatic mutation with 100% efficiency are not limitations to the pending claims. Therefore, there is sufficient expectation of success for the claimed invention based on the current claim language. Furthermore, the claimed invention is not made sooner does not necessarily mean that extraordinary skill is required to achieved the claimed invention. Even the invention is obvious and there is motivation to make the invention, the ordinary artisan does not have to reduce it to practice in short amount of time. As Applicants are fully aware that genetic manipulation of the mouse genome using the ES technology involves in vitro selection, blastocyst injection, implantation and successive mating of the chimeric mouse and transgenic mouse to obtain a homogenous background such that meaning analysis can be done. This process takes considerable amount of time. Four years is not an unusually long time which necessarily mean that extraordinary skill is required. As such, the claims as stand is obvious in view of the combined teaching of the cited references. Therefore, this rejection is maintained for same reasons discussed in the final office action. The proposed amendment overcomes the 112 2<sup>nd</sup> paragraph rejection of the record if entered.

  
**DAVE TRONG NGUYEN**  
**PRIMARY EXAMINER**